UOD-154US1

Appln. No.: 10/673,000

Amendment Dated: October 13, 2008

Reply to Advisory Action of September 4, 2008

<u>Amendments to the Claims:</u> This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

- 1. (Previously presented) A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of:
- (a) obtaining a sample comprising protein aggregates wherein the sample is substantially free of a denaturing agent;
- (b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of protein dissociates from said protein aggregates; and
- (c) returning the sample of step (b) to ambient pressure without repeatedly cycling the sample between the elevated and the ambient pressures, whereby a portion of the dissociated protein refolds to native protein.
- 2. (Original) The method of claim 1, wherein said protein aggregates are inclusion bodies.
- 3. (Previously Presented) The method of claim 1, wherein said elevated hydrostatic pressure is insufficient to fully denature said protein.
- 4. (Original) The method of claim 1, wherein said sample further comprises a chaotropic agent in an amount which is insufficient to denature said native protein at ambient pressure.
- 5. (Previously Presented) The method of claim 4, wherein said elevated hydrostatic pressure is insufficient to fully denature said protein.
- 6. (Original) The method of claim 5, wherein said protein aggregates are inclusion bodies.
- 7. (Previously presented) A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of:

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(a) obtaining a sample comprising protein aggregates wherein the sample is substantially free of a denaturing agent, and wherein said protein aggregates are comprised of protein folding intermediates of a native protein;

- (b) subjecting the sample of step (a) to elevated hydrostatic pressure, whereby a portion of said protein folding intermediates dissociate from said protein aggregates; and
- (c) returning the sample of step (b) to ambient pressure without repeatedly cycling the sample between the elevated and the ambient pressures, whereby a portion of the dissociated protein folding intermediates refold to native protein.
- 8. (Previously Presented) The method of claim 7, wherein said elevated hydrostatic pressure is insufficient to fully denature said protein folding intermediates.
- 9. (Original) The method of claim 7, wherein said protein aggregates are inclusion bodies.
- 10. (Original) The method of claim 7, wherein said sample further comprises a chaotropic agent in an amount which is insufficient to denature said native protein at ambient pressure.
- 11. (Previously Presented) The method of claim 10, wherein said elevated hydrostatic pressure is insufficient to fully denature said protein folding intermediates.
- 12. (Original) The method of claim 11, wherein said protein aggregates are inclusion bodies.
- 13. (Withdrawn) A method for recovering native protein from a sample comprising protein aggregates, said method comprising the steps of:
 - a. obtaining a sample comprising protein aggregates, wherein said protein aggregates are comprised of aggregation prone protein folding intermediates of a native protein;
 - subjecting said sample to a level of hydrostatic pressure sufficient to dissociate at least a portion of said aggregation prone protein folding intermediates contained in said protein aggregates; and
 - c. returning the sample of step (b) to ambient pressure, whereby a portion of the dissociated aggregation prone protein folding intermediates refold to native protein.

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14. (Withdrawn) The method of claim 13, wherein said elevated hydrostatic pressure is below the minimum level of hydrostatic pressure required to fully denature said aggregation prone protein folding intermediates.

- 15. (Withdrawn) The method of claim 13, wherein said protein aggregates are inclusion bodies.
- 16. (Withdrawn) The method of claim 13, wherein said sample further comprises a chaotropic agent in an amount which is insufficient to denature said native protein at ambient pressure.
- 17. (Withdrawn) The method of claim 16, wherein said elevated hydrostatic pressure is below the minimum level of hydrostatic pressure required to fully denature said aggregation prone protein folding intermediates.
- 18. (Withdrawn) The method of claim 17, wherein said protein aggregates are inclusion bodies.

19-20. (Cancelled)